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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/929,665	08/13/2001	Neil H. Bander	266/187	9976

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/929,665	BANDER, NEIL H.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2006, the Decision on Appeal*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *144,156-168 and 170-210* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144, 156-168, and 170-210* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20030602*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 144, 156-168, and 170-210, which are considered unpatentable for the reasons indicated below:

New Grounds of Objection

Drawings

2. The drawings set forth as Figures 8 and 11 are objected to because the figures depict amino acid sequences, which are not identified by sequence identification numbers, either in the figures or in the brief descriptions of figures at pages 12 and 13 of the specification, respectively. Sequences appearing in the specification and/or drawings must be identified by a sequence identifier in accordance with 37 C.F.R. 1.821(d); sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

A replacement drawing sheet, including the correction, is required, if the drawings are objected to. See 37 CFR 1.121(d). However, this ground of objection would be withdrawn, so that a replacement drawing would be not be required, if Applicant were to amend the brief description of the figure at page 4 of the specification to include sequence identification numbers.

Specification

3. The disclosure is objected to for the following reason: The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Sequences appearing in the specification and/or drawings must be identified by sequence identifier in accordance with 37 C.F.R. 1.821(d). According to 37 CFR § 1.821(a), an unbranched sequence of four or more specifically identified amino acids or an unbranched sequence of ten or more

nucleotides must be identified by sequence identification numbers. See MPEP § 2422.01.

In this instance, the sequences depicted in Figures 8 and 11 are not identified by sequence identification numbers, either in the figures or in the brief descriptions of figures at pages 12 and 13 of the specification, respectively.

Applicant must provide appropriate amendments to the specification or drawings inserting the required sequence identifiers. Sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

As noted in the attached Notice to Comply, appropriate action correcting this deficiency is required. If necessary to correct the deficiency, Applicant must submit paper and computer-readable copies of a substitute sequence listing, together with an amendment directing its entry into the specification and a statement that the content of both copies are the same and, where applicable, include no new matter.

4. The specification is objected to for the following reason:

At page 1, paragraph 1, of the specification there is a statement that this application is a continuation application of Application Serial No. 09/357,704, which is a divisional of Application Serial No. 08/836,682. The latter of these prior filed applications has since issued as U.S. Patent No. 6,107,090; yet the specification does not properly indicate the status of this application. Appropriate correction is required.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 144, 156-168, and 170-210 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** a monoclonal antibody selected from the group consisting of J591, J533, E99, and J415 produced by hybridomas deposited under ATCC deposit

accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively, an antigen-binding fragment thereof, a composition comprising said antibody or antigen-binding fragment, a kit for detecting prostate cancer comprising said antibody or antigen-binding fragment, and a hybridoma selected from the group consisting of the hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, *provided the deposit requirements are satisfied*, as explained below, **does not reasonably provide enablement for making and/or using** any antibody or antigen-binding fragment that competes for binding to PSMA with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533 and a J591 monoclonal antibody, an composition thereof, a kit for detecting any type of cancer comprising such an antibody or antigen-binding fragment thereof, or a cell that produces such an antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the

predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and./or unreasonable experimentation.

The determination that an antibody or antigen-binding fragment that competes for binding to PSMA with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533 and a J591 monoclonal antibody requires access to those antibodies. Moreover, the claimed invention cannot be made without those antibodies.

Although the specification describes the deposit of hybridomas in accordance with the Budapest Treaty, which produce monoclonal antibodies J591, J533, E99, and J415 (ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively), the specification does not teach one to make these antibodies by, for example, disclosing the entirety of their amino acid sequences or the polynucleotide sequences encoding their amino acid sequences. Notably, the specification teaches only the variable regions of the light and heavy chains of "J591" monoclonal antibodies (Example 12, paragraphs [0111]-[0126] of the published application), but such a disclosure would not be sufficient to enable the skilled artisan to reproduce the intact monoclonal antibody to which the claims are directed. Furthermore, it is unclear if a cell line (e.g., a hybridoma) that produces an antibody having the exact structural and chemical identity as any of J591, J533, E99, or J415 is known and publicly available, or can be reproducibly isolated without undue experimentation. Without access to a hybridoma or recombinant cell line producing the monoclonal antibodies to which the claims are directed, it would not be possible to make and/or use the claimed invention, because it would not be possible to make the antibody, and then use the antibody to determine if the claimed antibody or

antigen-binding fragment thereof competes for binding to PSMA with that antibody.

Furthermore, the claims are not necessarily limited to the antibodies or antigen-binding fragments that compete for binding to PSMA with an antibody produced by any of the deposited hybridomas; instead, the claims are more broadly directed to antibodies that compete for binding to PSMA with any of a *plurality* of "E99" monoclonal antibodies, any of a *plurality* of "J415" monoclonal antibodies, any of a *plurality* of "J533" monoclonal antibodies, or any of a *plurality* of "J591" monoclonal antibodies. It cannot be ascertained what "monoclonal antibodies" constitute each of the recited pluralities of monoclonal antibodies, as the specification fails to describe the particularly identifying structural and functional features of these pluralities; and one cannot make, what has not been described. If one cannot make the "monoclonal antibodies" to which the claims are directed, one cannot identify or select the claimed antibodies or antigen binding fragments thereof by determining whether or not candidate antibodies or antigen binding fragments thereof "compete" for binding to PSMA with those "monoclonal antibodies".

If the deposit requirements *were* satisfied, the disclosure would only be sufficient to make the monoclonal antibodies J591, J533, E99, and J415, which are produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively.

However, the referrals to deposits in the specification at, for example, paragraph [0087] of the published application, are insufficient assurance that all required deposits have been made and all the conditions of MPEP 608.01 (p)(c) are met. Although these deposits are described as having been made under the provisions of the Budapest Treaty (paragraph [0087] of the published application), Applicant has not provided the necessary assurance that that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

Therefore, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

Therefore, in conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 144, 156-168, 170-178, and 180-210 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-142 of U.S. Patent No. 7,045,605 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Claims 1-142 of the patent are directed to anti-PSMA antibodies or antigen binding fragments thereof, wherein said antibodies comprise the complementarity determining regions (CDRs) of any of monoclonal antibodies J591, J415, J533 and E99, or hybridomas, or other cell lines producing such antibodies. These antibodies bind to the same epitope(s) as monoclonal antibodies J591, J415, J533 and/or E99 and therefore "compete" for binding to PSMA with any one or more of those monoclonal antibodies.

Moreover, the claims of the patent are directed to such fragments of antibodies selected from the group consisting of Fab, $F(ab')_2$, Fv, and single chain Fv fragments.

The claims are also directed to such antibodies or antigen binding fragments thereof, which are coupled to a cytotoxic moiety selected from a

cytotoxic protein of plant, fungal, or bacterial origin, a radioisotope that emits alpha, beta, or gamma radiation, or a cytotoxic or therapeutic drug (e.g., a taxane).

The claims are also directed to such antibodies or antigen binding fragments thereof, which are coupled to a label selected from biologically active enzymes, prosthetic groups, luminescent materials, bioluminescent materials, fluorescent materials, paramagnetic materials and radioactive ions.

The radioisotopes to which the claimed antibodies or antigen binding fragments are coupled are selected from ^{212}Bi, ^{213}Bi, ^{211}At, ^{186}Re, ^{90}Y, ^{131}I, ^{32}P, ^{125}I, ^{3}H, ^{14}C, ^{188}Rh, and ^{99}mTc.

The claims of the patent are directed to pharmaceutical compositions comprising the antibodies or antigen binding fragments thereof and a pharmaceutically acceptable carrier, excipient, or stabilizer.

Although the claims of the patent are not expressly directed to antibodies or antigen binding fragments thereof that are internalized with PSMA, the specification teaches the claimed antibodies are internalized with PSMA and their internalization with PSMA by cells expressing PSMA is an inherent property of the interaction of those cells with such antibodies capable of internalization.

Otherwise the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

8. Claims 144, 156-168, 170-178, and 180-210 are directed to an invention not patentably distinct from claims 1-142 of commonly assigned U.S. Patent No. 7,045,605 B2. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in the above rejection of claims 144, 156-168, 170-178, and 180-210 on the ground of nonstatutory obviousness-type double patenting.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 7,045,605 B2, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

9. Claims 144, 156-168, 170-177, 180, 184-203, and 208-210 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21 and 52-137 of copending Application No. 10/379,838. Although the conflicting claims are not identical, they are not patentably distinct from each other the following reasons:

Copending claims 21 and 52-137 are directed to compositions comprising anti-PSMA antibodies or antigen binding fragments thereof, wherein said antibodies comprise the complementarity determining regions (CDRs) of monoclonal antibody J591. These antibodies bind to the same epitope as monoclonal antibody J591 and therefore "compete" for binding to PSMA with that monoclonal antibody.

Moreover, the copending claims are directed to such fragments of antibodies selected from the group consisting of Fab, $F(ab')_2$, Fv, and single chain Fv fragments.

The claims are also directed to such antibodies or antigen binding fragments thereof, which are coupled to a cytotoxic moiety selected from a cytotoxic protein of plant, fungal, or bacterial origin, a radioisotope that emits alpha, beta, or gamma radiation, or a cytotoxic or therapeutic drug (e.g., a taxane).

The claims are also directed to such antibodies or antigen binding fragments thereof, which are coupled to a label selected from biologically active enzymes, prosthetic groups, luminescent materials, bioluminescent materials, fluorescent materials, paramagnetic materials and radioactive ions.

The radioisotopes to which the claimed antibodies or antigen binding fragments are coupled are selected from ^{212}Bi, ^{213}Bi, ^{211}At, ^{186}Re, ^{90}Y, ^{131}I, ^{32}P, ^{125}I, ^{3}H, ^{14}C, ^{188}Rh, and ^{99}mTc.

The pharmaceutical or therapeutic compositions to which the copending claims are directed comprise the antibodies or antigen binding fragments thereof and a pharmaceutically acceptable carrier, excipient, or stabilizer.

Although the claims of the patent are not expressly directed to antibodies or antigen binding fragments thereof that are internalized with PSMA, the specification teaches the claimed antibodies are internalized with PSMA and their internalization with PSMA by cells expressing PSMA is an inherent property of the interaction of those cells with such antibodies capable of internalization.

Otherwise the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 144, 156-168, 170-177, 180, 184-203, and 208-210 are directed to an invention not patentably distinct from claims 21 and 52-137 of commonly assigned copending Application No. 10/379,838. Specifically, although the claims are not identical, they are not patentably distinct from each other for the reasons set forth in the above rejection of claims 144, 156-168, 170-177, 180, 184-203, and 208-210 on the ground of nonstatutory obviousness-type double patenting.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned copending Application No. 10/379,838, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
August 3, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

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